

Wyeth Ayerst Research
P.O. Box 8299
Philadelphia, Pa 19101-8299

23 FEB 2001

Attention: Nanette E. Holston
Associate Director
Global Brand Management, Regulatory Affairs

Dear Ms. Holston:

Please refer to your supplemental new drug application dated August 25, 2000, received August 28, 2000, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Phenergan with codeine (promethazine HCl and codeine phosphate) Syrup and Phenergan VC with codeine (promethazine HCl, phenylephrine HCl and codeine phosphate) Syrup.

This supplemental new drug application provides for a revision to the package insert in compliance with the Final Rule entitled "*Specific Requirements on Content and Format of Labeling for Human Prescription Drugs; Addition of 'Geriatric Use Subsection in Labeling'*", published on August 27, 1998, in the Federal Register (62 FR 45313-45326), which amended 21 CFR 201.57. Additionally, this supplement reflects the addition of the "Rx only" statement to the package insert.

We have completed the review of this supplemental application, as amended, and have concluded that adequate information has been presented to demonstrate that the drug products are safe and effective for use as recommended in the labeling text submitted August 25, 2000, and with the minor revisions listed below as agreed upon in a telephone conversation between you and Sandy Barnes of this Division on February 23, 2001. Accordingly, the supplemental application is approved, effective on the date of this letter.

For Phenergan with codeine (promethazine HCl and codeine phosphate) Syrup:

1. Revise the "**Geriatric Use**" subsection to read as follows:

Geriatric Use

Clinical studies of Phenergan formulations did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients. In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal or cardiac function, and of concomitant disease or other drug therapy.

Sedating drugs may cause confusion and over-sedation in the elderly; elderly patients generally should be started on low doses of Phenergan with Codeine Syrup and observed closely.

2. At Line 19, remove the hyphen from the phrase "methylmorphinan" such that the revised chemical name for codeine phosphate would read as follows: "(5", 6")-7,8-didehydro-4,5-epoxy-3-methoxy-17-methyl-morphinan-6-0l phosphate (1:1) (salt) hemihydrate"

For Phenergan VC with codeine (promethazine HCl, phenylephrine HCl and codeine phosphate) Syrup:

3. Revise the “**Geriatric Use**” subsection heading as follows:

Geriatric Use

Clinical studies of Phenergan formulations did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients. In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal or cardiac function, and of concomitant disease or other drug therapy.

Sedating drugs may cause confusion and over-sedation in the elderly; elderly patients generally should be started on low doses of Phenergan VC with Codeine Syrup and observed closely.

4. At Lines 108 and 109, use the Greek symbols “ α ” and “ β ” in the “**CLINICAL PHARMACOLOGY-Phenylephrine**” section, as appropriate, in favor of using “a” (for α) and “b” (for β).

The final printed labeling (FPL) must be identical to the respective package inserts submitted August 25, 2000, and include the minor revisions indicated. These revisions are terms of the approval of this application.

Please submit the copies of final printed labeling (FPL) electronically according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDA* (January 1999). Alternatively, you may submit 20 paper copies of the FPL as soon as it is available but no more than 30 days after it is printed. Please individually mount ten of the copies on heavyweight paper or similar material. For administrative purposes, this submission should be designated "FPL for approved supplement NDA 8-306/S-029." Approval of this submission by FDA is not required before the labeling is used.

If a letter communicating important information about this drug product (i.e., a "Dear Health Care Professional" letter) is issued to physicians and others responsible for patient care, we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH, HF-2
FDA
5600 Fishers Lane
Rockville, MD 20857

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, call Mr. David Hilfiker, Regulatory Project Manager, at (301) 827-1084.

Sincerely,

Robert J. Meyer, M.D.
Director
Division of Pulmonary and Allergy Drug Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research